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Public Meeting to Discuss SAN Trimer Cleanup Levels

Reich Farm Superfund Site

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Purpose of Meeting

- EPA plans to set a mandatory cleanup level for SAN Trimer in the Reich Farm Site's Soil and Groundwater
- The cleanup levels are based in part on animal testing performed by the National Toxicity Program (NTP)
- NTP will discuss and answer questions on their work.
- EPA will discuss and answer questions on how the cleanup levels were derived.

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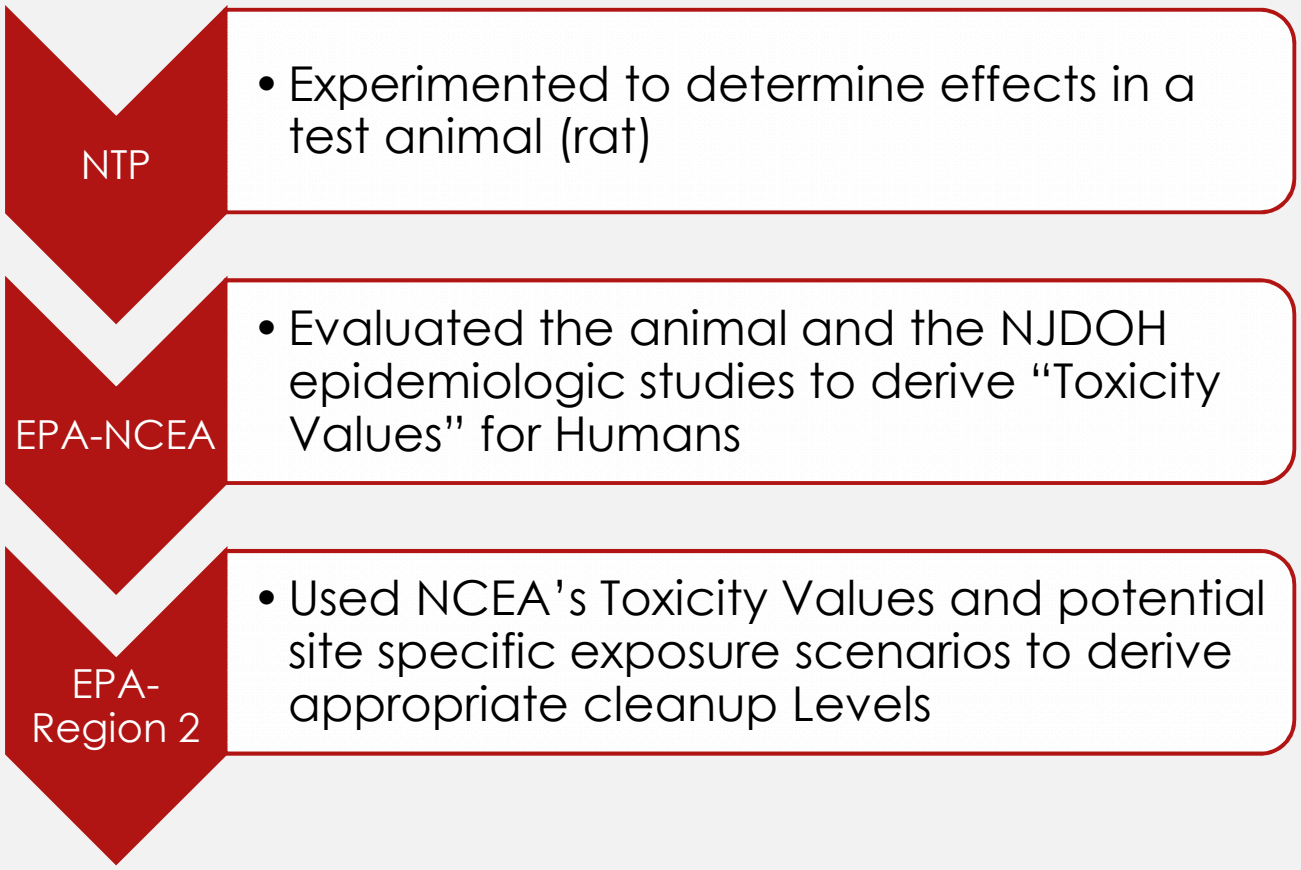

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The Reich Farm Superfund Site

A brief history

- Jon Gorin – Remedial Project Manager
- EPA Region 2

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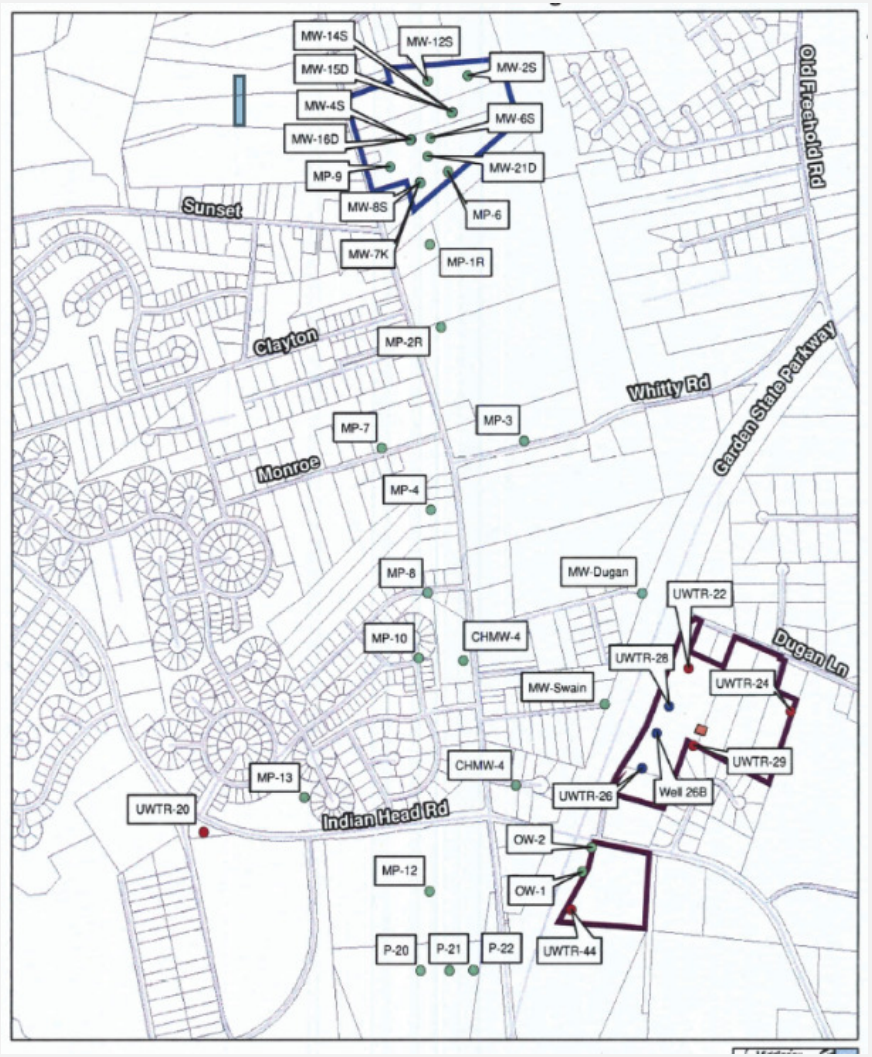
Site Location



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The Cause

- In 1971 Mr. Reich leased an unused portion of his farm to Mr. Fernicola.
- Fernicola is contracted by UCC to ship drums of waste material to a disposal area.
- Fernicola decides instead to dump waste on the Reich property

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Initial Actions

- The Reichs report the incident to authorities
- 1972 and 1974 UCC removes visible drums and grossly contaminated soil.
- 1974 the Dover Township Health Department issues a zoning ordinance restricting private well use around the Site.
- All residences and businesses within the area affected by the Site's contamination are connected to the public water supply

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EPA Gets Involved

- 1983 Reich Farm designated a Superfund site
- 1986 EPA begins a remedial investigation and feasibility study to evaluate the nature and extent of contamination
- Investigations confirm that soil and groundwater are contaminated
- 1988 EPA releases a Record of Decision (ROD) that required remedial action at the site

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ROD Requirements

- Additional groundwater and soil sampling to further delineate contamination related to the Site;
- Excavation and treatment of contaminated soil by enhanced volatilization (thermal desorption) to remove organic compounds down to NJ soil action levels; and
- Installation of a groundwater pumping, treatment and reinjection system to remove contaminants from groundwater until state and federal cleanup standards are met.

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Post ROD Work Begins

- 1989 EPA and UCC sign a consent decree that requires UCC to design and construct the cleanup as described in the 1988 ROD
  - First step: Additional groundwater/soil sampling

- Based on the additional soil sampling, EPA concluded that:
  - The volume of contaminated soils at the Site was approximately 15,000 cubic yards.

Treatment of the contaminated soil completed in 1995.

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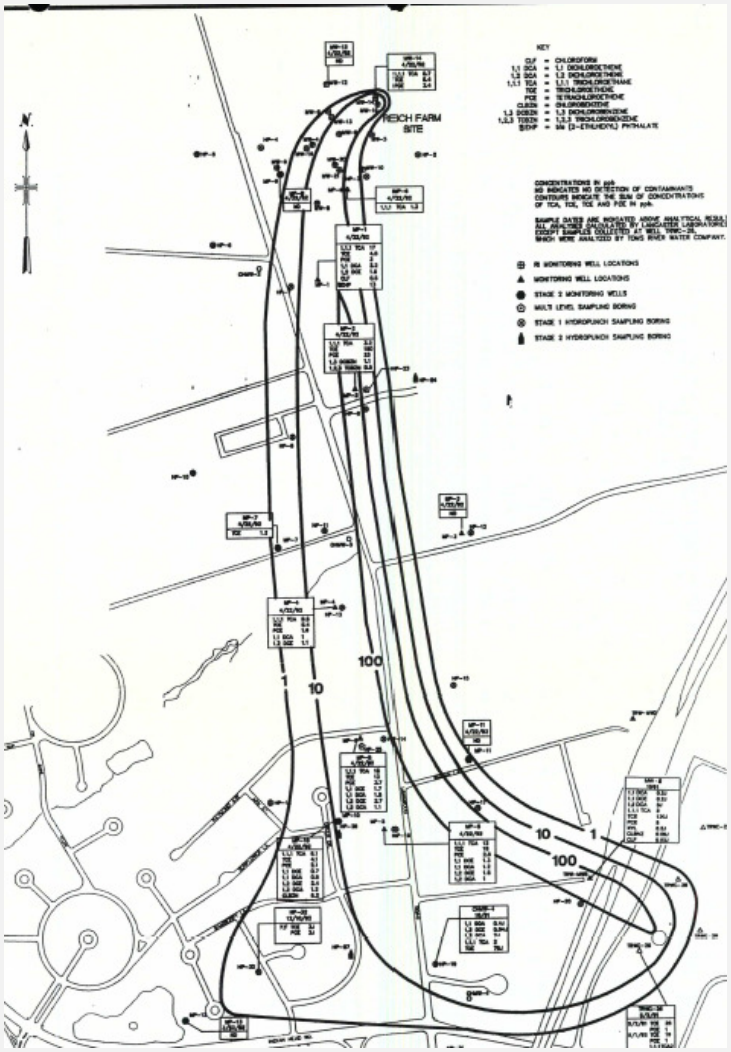
UCC Pre-design Groundwater Sampling:

Confirmed that the groundwater contamination at the Parkway Well Field was Site related



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EPA modifies groundwater remedy
First ESD

- EPA decided that an upgradient treatment plant would not:
  - significantly decrease the overall groundwater cleanup time or
  - prevent most of the mass from reaching the Well Field.

- 1995 – EPA issued an Explanation of Significant Differences (ESD) *[ESD=ROD change]* to allow the continued capture and treatment of the groundwater plume at the Parkway Well Field.

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Discovery of the SAN Trimer

- In 1996, New Jersey's Dept. of Health (NJDOH) found an increased incidence of childhood cancers in Toms River for the years 1979-1991.
- NJDOH began an analysis of various potential environmental causes of the elevated cancer rates.
- The presence of a group of unregulated, previously unknown contaminants was noted in the Site's groundwater plume.
- These contaminants, which are Site related, were identified and are now referred to collectively as the SAN Trimer.

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SAN Trimer

- Byproduct in manufacture of styrene-acrylonitrile polymers by specific process used at UCC facility.
- Present at low part per billion (ppb) levels in the same Well Field wells known to be impacted by other Site contaminants.
- Existing well field treatment system ineffective at removing SAN Trimer.
- No toxicity information existed for the chemical.

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Addressing the SAN Trimer

First Steps and Second ESD

- 1996 Contaminated wells “turned off”
- 1997 UCC adds additional treatment to remove SAN Trimer
  - Treated water is discharged to the ground rather than used as drinking water
- 1998 - EPA issues Second ESD requiring:
  - Removal of SAN Trimer to the interim cleanup level of less than the laboratory detection limit (<100 parts per trillion in 1998).
  - The interim cleanup level to remain in place until toxicity studies provide enough information for the development of a risk based cleanup level.

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SAN Trimer Workgroup Membership

- Federal government
  - EPA
  - Agency for Toxic Substances and Disease Registry (ATSDR)
  - NTP
- State government (New Jersey)
  - Department of Environmental Protection
  - Department of Health
- Industry
  - Union Carbide Corporation (i.e., Dow)
- Public
  - Citizen's Action Committee on Childhood Cancer Cluster

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SAN Trimer Testing

- Congressman asks the National Toxicology Program (NTP) to consider appropriateness of testing SAN Trimer in pregnant rats and their offspring.

- NTP agrees to perform testing.

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NJDOH/ATSDR Case Control Studies

NJDOH/ATSDR conduct a “case control” study to determine if there’s a relationship between exposure pathways and elevated cancer rates.

- Contamination at the Parkway Well Field (Reich)
- Contamination at the Holly Well Field (Ciba-Geigy Superfund Site)
- Air emissions (Ciba)
- Proximity to the Superfund Sites, the Ciba pipeline and to Dover & Ocean County landfills

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Case Control Study Results (2003)

- No associations found between pre or postnatal exposures and brain or central nervous system cancer in either males or females.
- No association found between postnatal exposures and leukemia in males or females
- No association found between prenatal exposures and leukemia in males
- Association found between prenatal exposure to Parkway well water and Ciba air exposure for leukemia in girls
  - "Considerable uncertainties"

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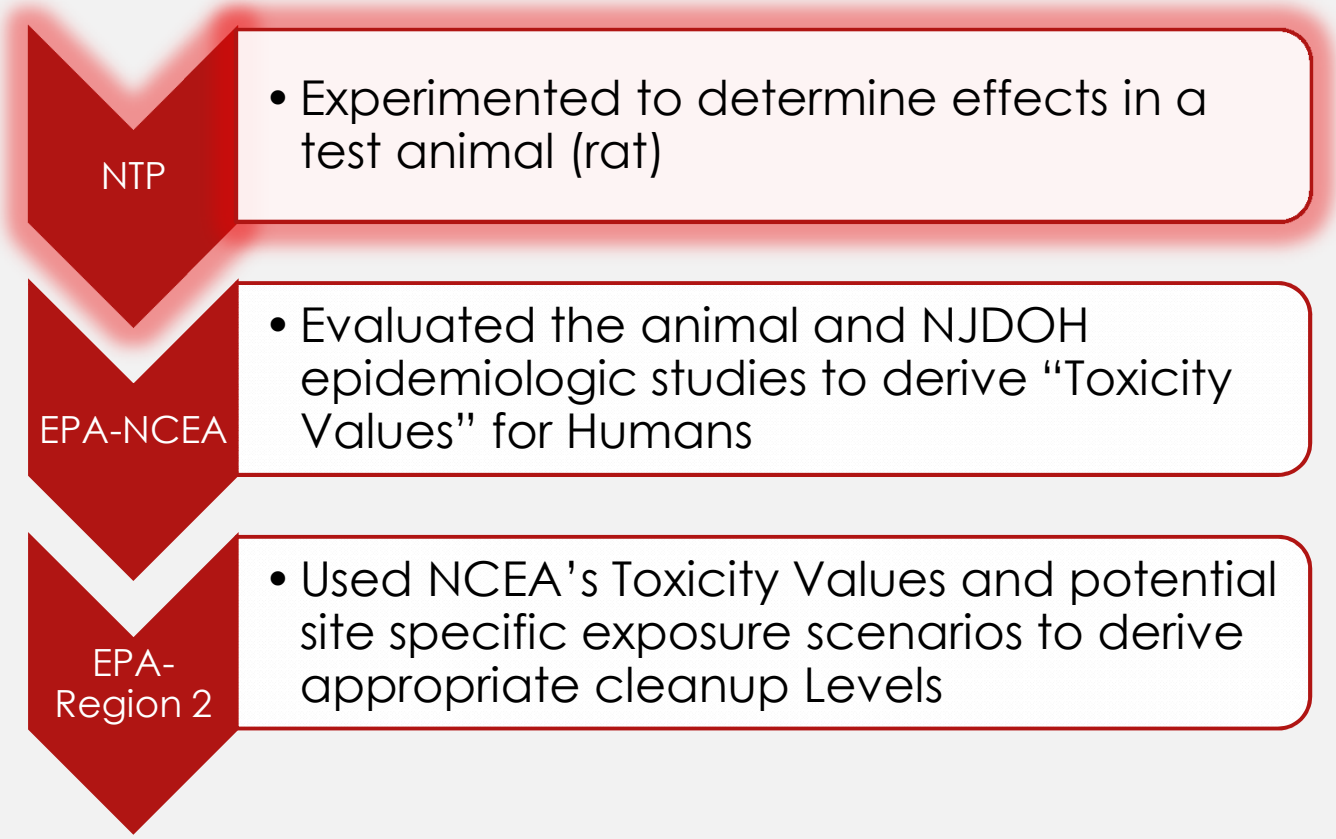


NTP
National Toxicology Program

Rat Studies on SAN Trimer

Mamta Behl, Ph.D. DABT
Study Scientist

Susan A. Elmore, DVM, DACVP, DABT, FIATP
Study Pathologist

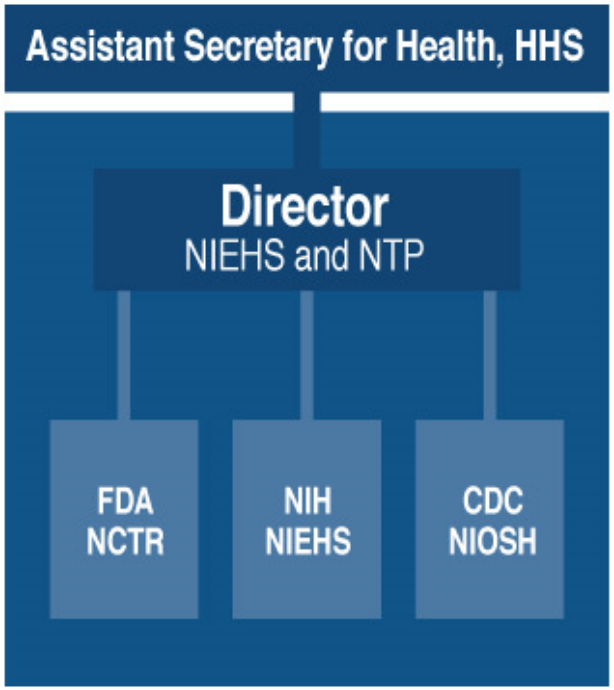
Division of the National Toxicology Program
National Institute of Environmental Health Sciences
Research Triangle Park, North Carolina, USA

Outline

- NTP
  - Background
  - NTP study process
  - NTP process for evaluation of carcinogenicity
- SAN Trimer
  - Nomination and timeline of activities
  - SAN Trimer workgroup
  - Study design and endpoints
  - 2-Year bioassay results
  - Pathology evaluation
  - Conclusions

National Toxicology Program (NTP)

- NTP is an interagency program
- NTP was established in 1978 and is headquartered at National Institute of Environmental Health Sciences (NIEHS)
- Goal: to safeguard the public by identifying substances in the environment that may affect human health
  - Coordinate toxicology testing programs across the federal government

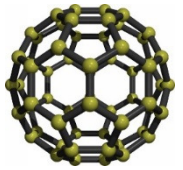


http://ntp.niehs.nih.gov

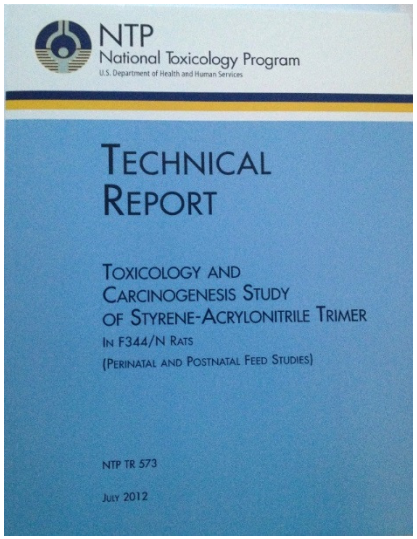
Areas for NTP Research and Testing

- Consumer products
  - Cell phone radiation, sunscreen components, flame retardants, nanomaterials, plastics, bisphenol A
- Our surroundings/environment
  - Mold, food borne toxicants/carcinogens, Elk River spill, drinking water and groundwater contaminants
- Medicines and therapeutics
  - AIDS therapeutics, dietary supplements, and botanicals
- Workplace exposures
  - Butter flavorings, metal working fluids, nanomaterials





NTP Study Process



Environmental groups, academia, state and federal agencies, labor unions, public → Chemical Nomination

Chemists, pathologists, toxicologists, and statisticians → Design studies

Conduct animal studies

Pathology peer review →

Prepare technical report

Draft conclusions

Public input → Expert panel peer review: public meeting & comment

NTP staff finalizes conclusion

NTP Director approves report

Final NTP conclusions published

Rigorous process with checks and balances at multiple stages

Peer Review Panel

- Selected by NTP Leadership amongst outstanding experts in relevant scientific disciplines
- Followed Federal policies and requirements
- Comprised of experts from industry and academia to ensure balanced representation
- Screened for conflict of interest
- Provided all written public comments *apriori* to panel
- Input was considered advisory; final conclusions made by NTP staff

NTP Levels of Evidence of Carcinogenic Activity

Under the conditions of the study….

- **Clear evidence of carcinogenic activity**
- **Some evidence of carcinogenic activity**

POSITIVE

- **Equivocal evidence of carcinogenic activity**

UNCERTAIN

- **No evidence of carcinogenic activity**

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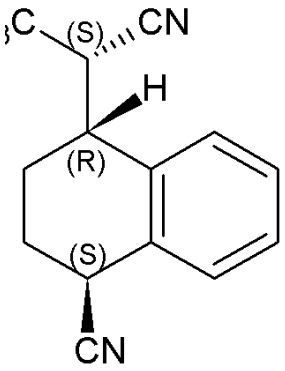
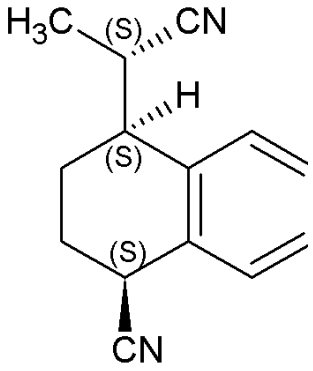
What is SAN Trimer?

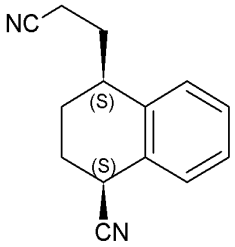


Cis-R-THNA

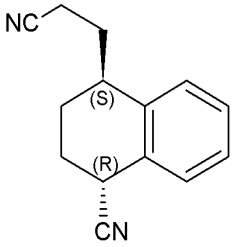


Cis-S-THNA

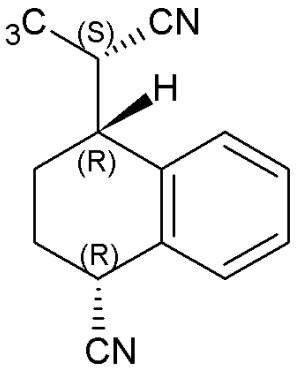
Molecular weight = 210
Chemical Formula: $C_{14}H_{14}N_2$



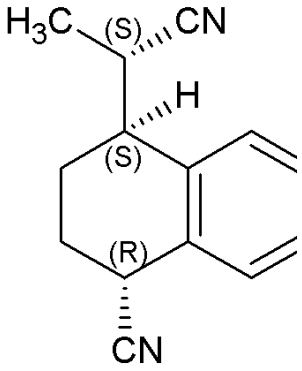
Cis-THNP



Trans-THNP



Trans-R-THNA



Trans-S-THN

- Chemical Mixture
- By-product of a specific production process of polymerization

NTP Findings and Conclusions

- NTP conducted studies on SAN Trimer in rats
- NTP concluded that SAN Trimer did not cause cancer in male or female rats
- Other non-cancer effects noted were:
  - Peripheral nerve degeneration
  - Effects on liver, bone marrow and urinary bladder

Nomination and Activities for SAN Trimer

- Congressman Saxton (NJ) requests that NTP consider testing SAN Trimer for potential carcinogenicity
- NTP agrees to perform testing – 1997
- SAN Trimer Workgroup established – 1997
- EPA requests that NTP join the Workgroup – 1998
- NTP studies start – 2000
  - Chemical procurement
  - 7-week, 18-week, 2-year studies
- Peer Review – 2011
- Publication of final NTP Technical Report – 2012

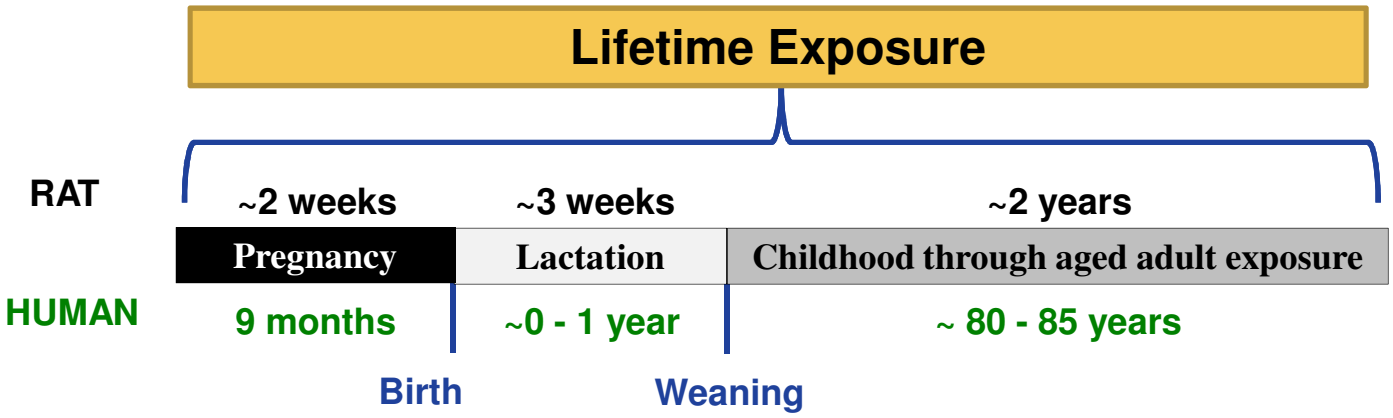
SAN Trimer Workgroup Membership

- Federal government
  - Environmental Protection Agency – Region 2/headquarters
  - Agency for Toxic Substances and Disease Registry
  - **NTP**
- New Jersey government
  - Department of Environmental Protection
  - Department of Health and Senior Services
- Union Carbide Corporation (now Dow)
- Citizens Action Committee on Childhood Cancer Cluster

NTP and Workgroup Roles

- NTP responsible for the design and conduct of rat studies
  - Workgroup provided input and feedback on design of the studies
  - Workgroup selected dose levels for the 18-week and 2-year studies of SAN Trimer in feed
- NTP responsible for data evaluation interpretation and conclusions of rat studies
- NTP updated the Workgroup periodically on the progress throughout conduct of all rat studies and data evaluation

2-Year Bioassay



2 sexes x 4 groups x 50 rats/group = 400 rats

Does SAN Trimer cause cancer or other toxic effects in rats following lifetime exposure starting in the womb?

2-Year Bioassay

Model: F344/N rats

- Suitable for developmental exposure
- Sensitive to detection of central nervous system tumors
- Historical control database

Exposure: 2 years starting *in utero* (in the womb)

- Considered sensitive to nervous system toxicity and carcinogenicity
- Captures relevant period of exposure in children

Concentrations tested: 0, 400, 800, 1600 ppm in feed

- Preliminary 7-week and 18-week studies were conducted to set doses for the 2-year bioassay

2-Year Bioassay

- Currently the gold standard for identifying potential human carcinogens
- All known human carcinogens cause cancer in rodents
- Findings used by regulatory authorities for risk assessment and regulation

Endpoints Evaluated in 2-Year Bioassay

- Survival
- Body weight
- Reproductive parameters
- Clinical observations (e.g., behavior, activity, grooming)
- Clinical chemistry and hematology
- Microscopic evaluation of tissues
  - ~40 tissues/ animal X 400 animals = 16000 tissues!

Comprehensive assessment of SAN Trimer exposure

2-Year Study Results

- No effect on survival
- Rats in highest exposure group weighed 15% less than controls
- No effects on pregnancy and littering
- No toxicologically relevant effects on clinical chemistry and hematology
- No significant increase in cancer
- Non cancer effects on liver, bone marrow of exposed males and females, and urinary bladder of exposed females
- Non cancer effects in peripheral nerves of exposed males and females

Since the nervous system was a potential target for cancer, the NTP conducted a more detailed evaluation of the brain and spinal cord than typically done in 2-year studies

Pathology Overview

- NTP pathology peer-review process
- Central and peripheral nervous system evaluation and results
- NTP study conclusions

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Workflow for NTP Peer Review of Pathology

Study Lab Pathologist

↓

Quality Assessment Pathologist

↓

Pathology Working Group Pathologist

↓

Pathology Working Group

Multilevel pathology review: Ensures the quality, accuracy and confidence in the pathology data from NTP studies

Pathology Overview

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Central and Peripheral Nervous System Evaluations

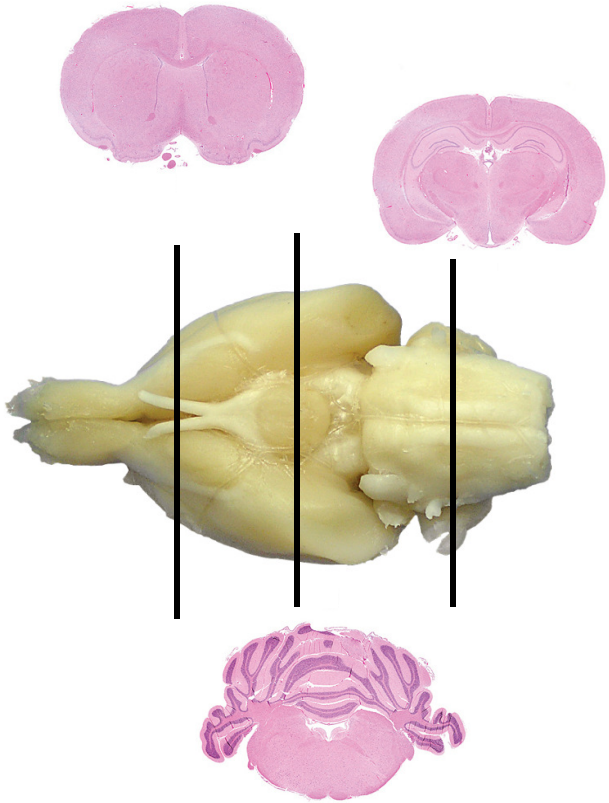
- A special review of central and peripheral nervous system tissue was performed in addition to the standard review of tissues from the 2-year study
  - The potential relationship between SAN Trimer and central nervous system (CNS) tumors in children
  - Thorough evaluation to identify all tumors or other lesions
- CNS evaluation included brain and spinal cord
- Peripheral nervous system evaluation included spinal nerve roots and sciatic nerves

Brain Tissue Sections Evaluated

Standard review: 3 sections of brain tissue

Special review: 9 additional sections of brain tissue

Total sections of brain tissue evaluated: 12



Spinal Cord Sections Evaluated

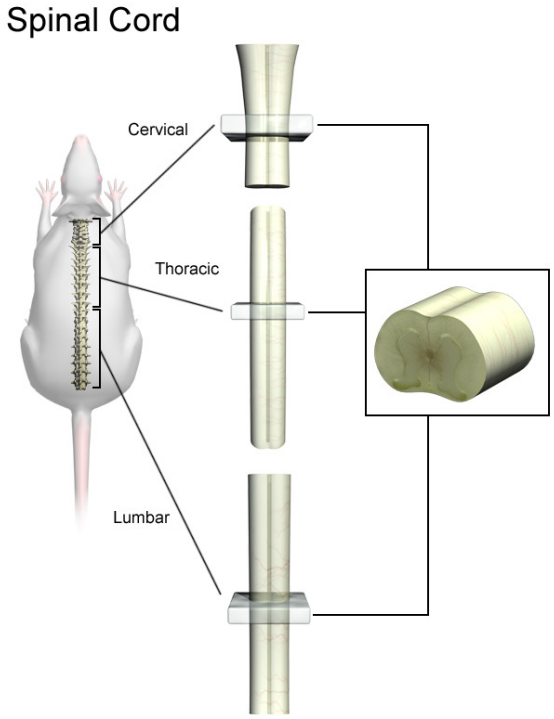
Standard review: not examined unless there was a grossly visible lesion (can see without a microscope) or clinical signs

Special review: evaluated multiple regions of the spinal cord

Cervical: neck region

Thoracic: mid back region

Lumbar: lower back region



Control Data From Untreated Rats

- Aging animals will show health effects and background tumors even if not treated
- To determine if the tumors in treated rats are due to age or treatment, compare the tumor numbers from treated rats to those of untreated rats
- Untreated rats within a study called “control group”; compare treated groups to this untreated group
- “Historical control data” is tumor data from untreated control rats from other 2-year NTP studies that were done over the past 5 years

Brain and Spinal Cord Review Results

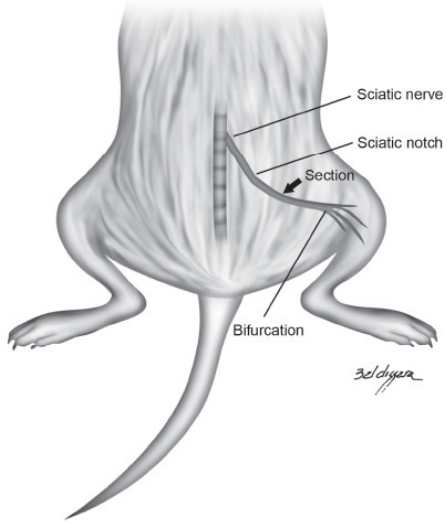
Considering both the historical control data and the untreated controls within the study,

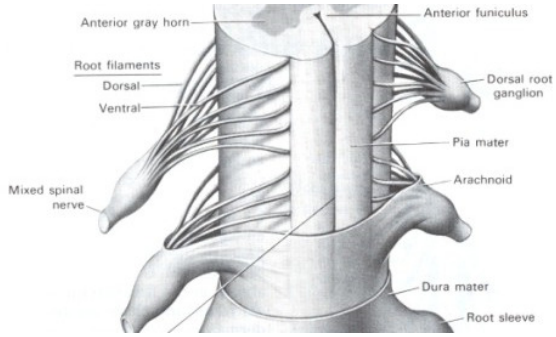
- The NTP did not find a dose-related increase in brain or spinal cord tumors beyond what was considered a function of normal aging

Peripheral Nerve Sections Evaluated

- Sciatic nerves
  - Major nerves in the hind limbs
  - **Standard review:** not examined
  - **Special review:** both the right and left sciatic nerves

- Spinal nerve roots
  - Nerve fiber bundles that emerge from either side of the spinal cord
  - **Standard review:** not examined
  - **Special review:** examined





http://neurosurgerycns.wordpress.com/tag/rat-sciatic-nerve/

http://rws2012.wordpress.com/brain/the-nervous-system

Peripheral Nerve Degeneration Results

- Peripheral nerve degeneration is a common age-related lesion in rats
- An increase in the incidence and/or severity of sciatic nerve and spinal nerve root degeneration in male and female rats when compared to untreated controls

	0ppm	400ppm	800ppm	1600ppm
Females				
Degeneration of sciatic nerve fibers (percentages)	57	71	88**	80**

**Significantly different ($p \leq 0.01$) from the control group by the Poly-3 test

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NTP Levels of Evidence of Carcinogenic Activity

Under the conditions of the study….

- **Clear evidence of carcinogenic activity**
- **Some evidence of carcinogenic activity**

POSITIVE

- **Equivocal evidence of carcinogenic activity**

UNCERTAIN

- **No evidence of carcinogenic activity**

Call for This Study: Rationale

- The NTP draft report proposed "equivocal evidence" of carcinogenic activity in male rats and "no evidence" in female rats
- The NTP made a final call of "no evidence" of carcinogenic activity after considering the study data and the discussions and recommendations by the external Peer Review Panel
- The final NTP call was supported by:
  - Incidences of brain and spinal cord tumors were low and not significantly different from the study controls
  - Incidence of brain tumors was consistent with background incidence (untreated controls) in rats from other NTP studies
  - No additional brain tumors were found in the special review

NTP Study Conclusions

- NTP concluded that, under the conditions of this study, SAN Trimer did not cause cancer in male or female rats
- NTP also reported:
  - Peripheral nerve degeneration: sciatic and spinal nerve roots
  - Non-neoplastic effects: liver, bone marrow, urinary bladder
  - Decreased tumors: pituitary gland, mammary gland, and mononuclear cell leukemia

http://ntp.niehs.nih.gov/go/36150

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journal homepage: www.elsevier.com/locate/toxicol

Perinatal toxicity and carcinogenicity studies of styrene-acrylonitrile trimer, a ground water contaminant

Mamta Behl[a,b,*], Susan A. Elmore[b], David E. Malarkey[b], Milton R. Hejtmancik[c], Diane K. Gerken[c], Rajendra S. Chhabra[b]

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5 MINUTE BREAK

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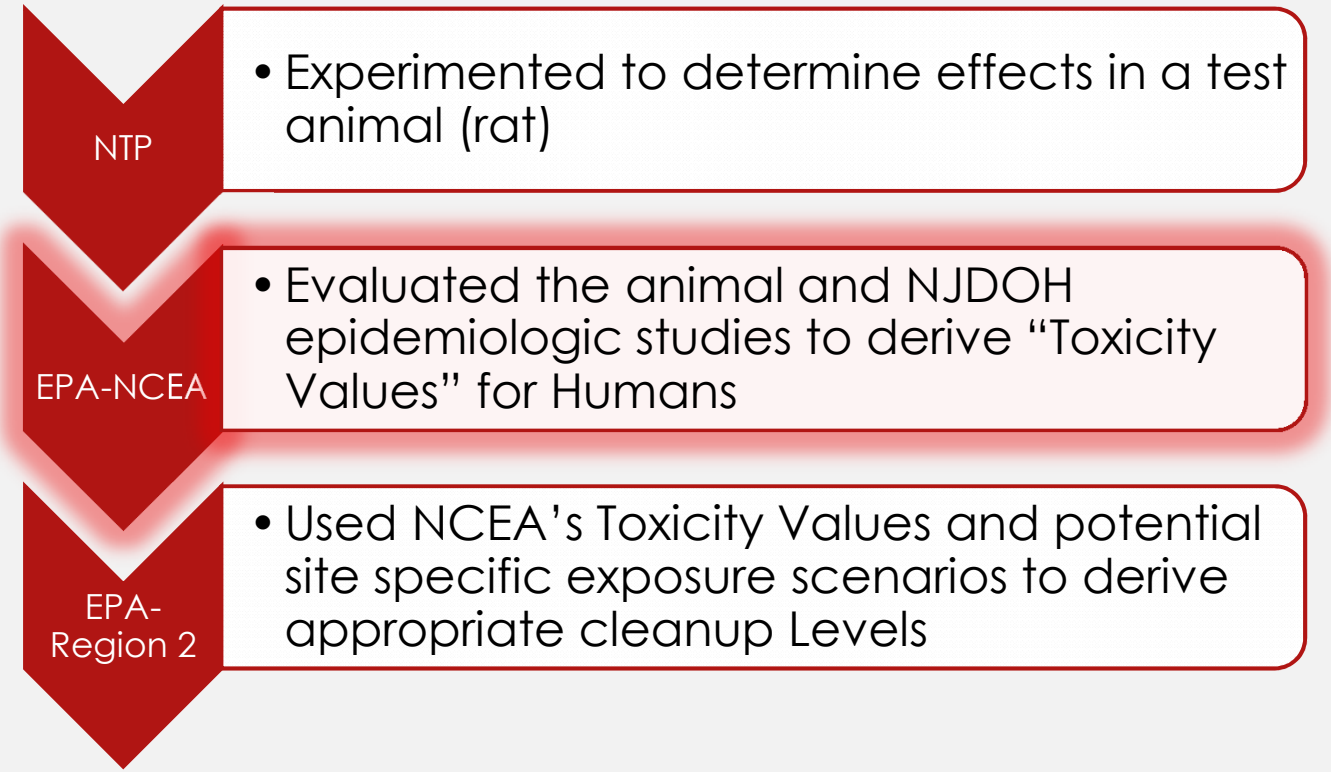

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U.S. EPA's Provisional Peer-Reviewed Toxicity Value (PPRTV) Assessment for SAN Trimer

Scott Wesselkamper, Ph.D. (Biologist, NCEA, Cincinnati, OH)

Annette Gatchett (Division Director, NCEA, Cincinnati, OH)

Lynn Flowers, Ph.D., DABT (Associate Director for Health, NCEA, Washington, DC)

Office of Research and Development
National Center for Environmental Assessment

February 4, 2015

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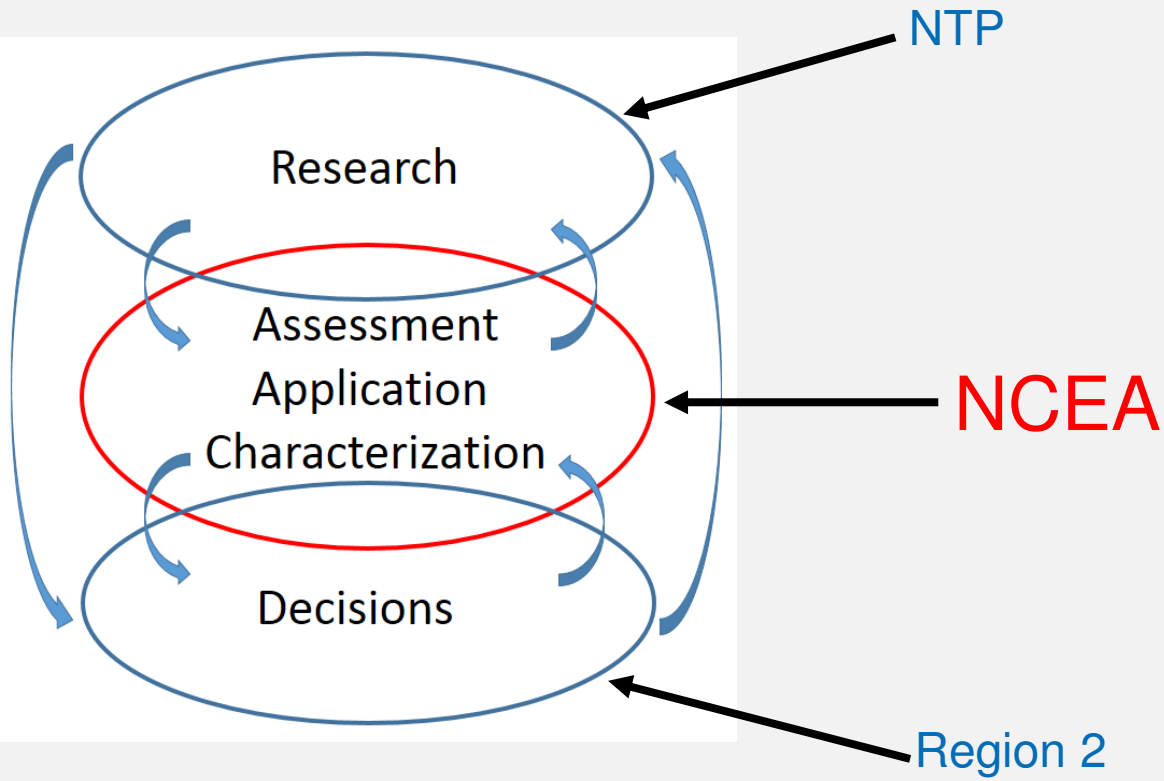
Presentation Overview

- Background information – National Center for Environmental Assessment (NCEA) and the Human Health Risk Assessment Program
- Development of health assessments
- General information – Provisional Peer-Reviewed Toxicity Value (PPRTV) assessments
- SAN Trimer PPRTV assessment process
- Summary of noncancer toxicity values for SAN Trimer
- Summary of cancer weight-of-evidence descriptor for SAN Trimer

U.S. EPA's NCEA is at the Interface of Environmental Decision-Making and the Scientific Research Community



- NCEA's Human Health Risk Assessment Program supports risk-based decisions made by EPA, state/local/tribal agencies, and the public to protect public health and the environment that are based on reliable, transparent, and high-quality risk assessment methods, models, and data.
- NCEA's scientists are recognized internationally for their expertise in toxicology, epidemiology, biology, chemistry and statistics. NCEA scientists serve on many federal government workgroups that are addressing critical environmental challenges and questions.

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What Is a Health Assessment?

- Depending on the available data, health assessments may include information on:
  - An estimate of the amount of a chemical that people can be exposed to daily (including susceptible people) that is likely to be without harmful health effects.
  - The potential for a chemical to cause cancer in people.

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Use of PPRTV Assessments

- The Superfund Technical Support Center (STSC) within NCEA-Cincinnati develops PPRTV assessments for use by the Superfund Program.
- PPRTV assessments are based on the same methods, sources of data and guidance for toxicity value derivation used by EPA's Integrated Risk Information System (IRIS) Program.

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SAN Trimer PPRTV Assessment Process

Date	Milestone
Dec. 2011	EPA's Region 2 requested that a PPRTV assessment be developed for SAN Trimer
Jul. 2012	NTP report on SAN Trimer was finalized
Jul. 2012	NCEA internal review of draft PPRTV assessment
Sep. 2013	Draft PPRTV assessment underwent external peer review by five independent scientific experts
Aug. 2014	PPRTV assessment was finalized

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Expert Peer Review Process for the SAN Trimer PPRTV Assessment

- Expert peer review is the cornerstone of EPA science.
- PPRTV assessments undergo a rigorous quality assurance process and peer review:

  1) NCEA panel review,

  2) External peer review by independently selected scientific experts, and

  3) NCEA final review.
- Peer reviewers for the SAN Trimer PPRTV assessment were selected and screened for any conflicts of interest by Eastern Research Group, Inc.

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Expert Peer Review Process for the SAN Trimer PPRTV Assessment (cont.)

- The five external peer reviewers are listed below, along with their respective expertise:
  - Lucio G. Costa, Ph.D. (neurotoxicology), Professor, Department of Environmental and Occupational Health Sciences, University of Washington, Seattle, WA
  - Julie E. Goodman, Ph.D., DABT (epidemiology), Principal, Gradient, Cambridge, MA
  - Annette Iannucci, M.S., DABT (general toxicology), Department of Labor, OSHA, Washington, DC (review conducted as independent consultant)
  - Martin A. Philbert, Ph.D. (neurotoxicology/neurocarcinogenesis), Dean and Professor of Toxicology, School of Public Health, University of Michigan, Ann Arbor, MI
  - Jerry M. Rice, Ph.D. (carcinogenesis), Distinguished Professor of Oncology and Member of the Cancer Prevention and Control Program, Lombardi Comprehensive Cancer Center, Georgetown University Medical Center, Washington, DC

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Main Features of the SAN Trimer Human Database (NJDOH/ATSDR Studies)

- Cancer Registry Analysis (1997):
  - NJDOH confirmed the childhood cancer incidence between 1979–1995 was statistically significantly elevated primarily due to leukemia and brain/central nervous system cancers in females under five years of age residing in the Toms River section of Dover Township.
- Case-Control Analysis (2003):
  - No associations found between exposures (pre- or postnatal) and brain or central nervous system cancer in either male or female children.
  - No association found between postnatal exposures and leukemia in male or female children.
  - No association found between prenatal exposures and leukemia in male children.
  - Statistically significant association found between prenatal exposure to Parkway well water (1982–1996) and leukemia in females ≤ 19 years of age.

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Evaluation of SAN Trimer Human Toxicity Database

- The existence of other contaminants in drinking water from the well fields investigated limit the conclusions that can be drawn from the epidemiologic studies.

- Some of the other chemicals that were present in the drinking water (e.g., trichloroethylene and tetrachloroethylene) are known to be carcinogens.

- If SAN Trimer were determined to have carcinogenic potential, the information necessary to establish a dose-response relationship from the human studies is absent because SAN Trimer concentrations in the drinking water were not measured as part of these studies.

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Evaluation of the SAN Trimer Animal Database

- Cancer:
  - Brain and spinal cord astrocytomas and granular cell tumors in male rats were found at the two highest doses in the 2-year cancer bioassay conducted by NTP, but they were not statistically significantly increased and were within historical control ranges.

- Noncancer:
  - Several effects were observed in the 2-year study, including nervous system effects consisting of sciatic nerve degeneration and spinal root degeneration; also liver, bone marrow, and bladder effects.

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Chronic Noncancer Oral RfD

Version	Principal Study / Critical Effect(s)	Low Dose (mg/kg-day)	UFs	RfD (mg/kg-day)
External Peer Review Draft PPRTV Assessment	NTP (2012); 104-week feeding study in F344 rats Increased incidence of chronic active inflammation in the liver of male rats	0.77	300 $UF_A = 3$ $UF_D = 10$ $UF_H = 10$	0.003
Final PPRTV Assessment	NTP (2012); 104-week feeding study in F344 rats Increased incidences of chronic active inflammation in the liver of male rats and sciatic nerve degeneration in female rats	0.77	300 $UF_A = 3$ $UF_D = 10$ $UF_H = 10$	0.003

Reference Dose (noncancer): An estimate of the amount of a chemical that people (including sensitive people) can be exposed to daily that is likely to be without harmful health effects.

RfD = low dose with little or no adverse effect ÷ uncertainty factors*

*applied to account for human variability, extrapolating from animals to humans, and database deficiencies.

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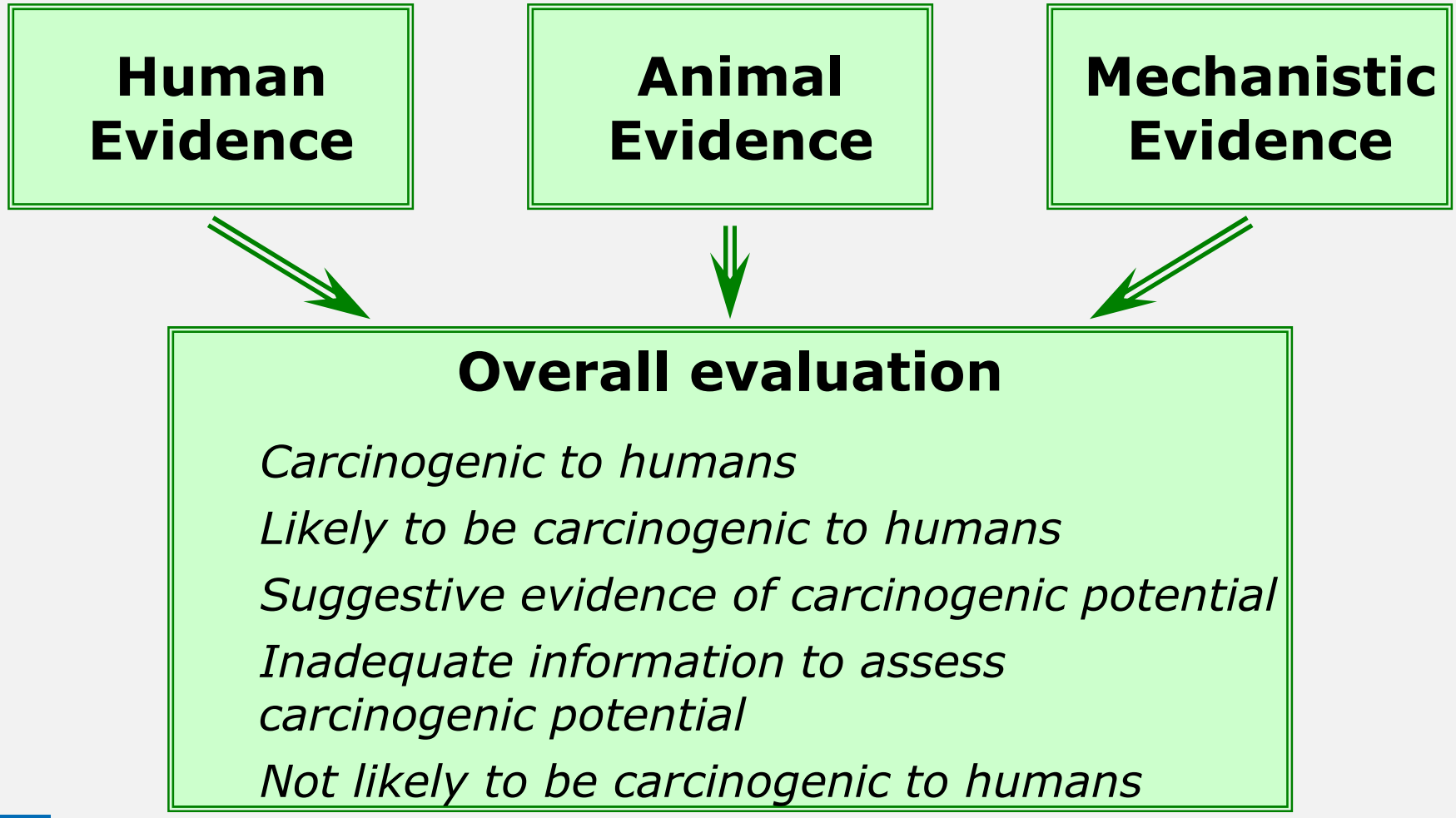
Cancer Descriptors Integrate Human, Animal, and Mechanistic Evidence (2005 U.S. EPA Cancer Guidelines)



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Cancer Weight-of-Evidence Descriptor and Estimation of Cancer Risk – External Peer Review Draft

Version	Cancer Descriptor	Screening level cancer risk estimate
External Peer Review Draft PPRTV Assessment	*Suggestive evidence of carcinogenic potential* [borderline case between *suggestive evidence* and *inadequate evidence*]	Calculated based on the incidence of brain and spinal cord astrocytomas in male rats (NTP, 2012)

Examples:

- *Inadequate information to assess carcinogenic potential*: Little or no information; negative results but lacking a robust database.
- *Suggestive evidence of carcinogenic potential*: Small, and possibly not statistically significant, increase in tumors; increase in tumors at one dose and not another.

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External Peer Review Comments on the Cancer Descriptor

- One reviewer agreed with the cancer descriptor indicating *suggestive evidence of carcinogenic potential*.
- One reviewer indicated the descriptor indicating *suggestive evidence* was acceptable, but that if there was a scale within the category, SAN Trimer would be at the bottom and closer to the descriptor indicating that there was *inadequate information to assess the carcinogenic potential*.
- One reviewer commented that the most applicable cancer descriptor was that there is *inadequate information to assess the carcinogenic potential.*
- Another reviewer indicated that the best descriptor would be that SAN Trimer is *not likely to be carcinogenic to humans*, but since there is very limited human data, one might say that there is *inadequate information to address the carcinogenic potential*.
- One reviewer did not comment specifically on the choice of the descriptor but indicated that there was a paucity of available data and that estimation of cancer risk under these circumstances would be fraught with uncertainty.

Cancer Weight-of-Evidence Descriptor and Estimation of Cancer Risk – Final Assessment

Version	Cancer Descriptor	Screening level cancer risk estimate
External Peer Review Draft PPRTV Assessment	*Suggestive evidence of carcinogenic potential* [borderline case between *suggestive evidence* and *inadequate evidence*]	Calculated based on the incidence of brain and spinal cord astrocytomas in male rats (NTP, 2012)
Final PPRTV Assessment	*Inadequate evidence to determine the carcinogenic potential* [borderline case between *suggestive evidence* and *inadequate evidence*]	None

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External Peer Review Comments on the Derivation of a Screening Level Cancer Risk Estimate

- One reviewer agreed with the derivation of the cancer risk estimate.
- Three reviewers stated that a cancer risk estimate should not be derived.
- One reviewer did not explicitly recommend that the cancer risk estimate be removed from the assessment, but stated that the derivation would be fraught with uncertainty if retained.

Cancer Weight-of-Evidence Descriptor and Estimation of Cancer Risk – Final Assessment

Version	Cancer Descriptor	Screening level cancer risk estimate
External Peer Review Draft PPRTV Assessment	*Suggestive evidence of carcinogenic potential* [borderline case between *suggestive evidence* and *inadequate evidence*]	Calculated based on the incidence of brain and spinal cord astrocytomas in male rats (NTP, 2012)
Final PPRTV Assessment	*Inadequate evidence to determine the carcinogenic potential* [borderline case between *suggestive evidence* and *inadequate evidence*]	None

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- Teresa Shannon: STSC Administrator
- Eastern Research Group: External Peer Review Services

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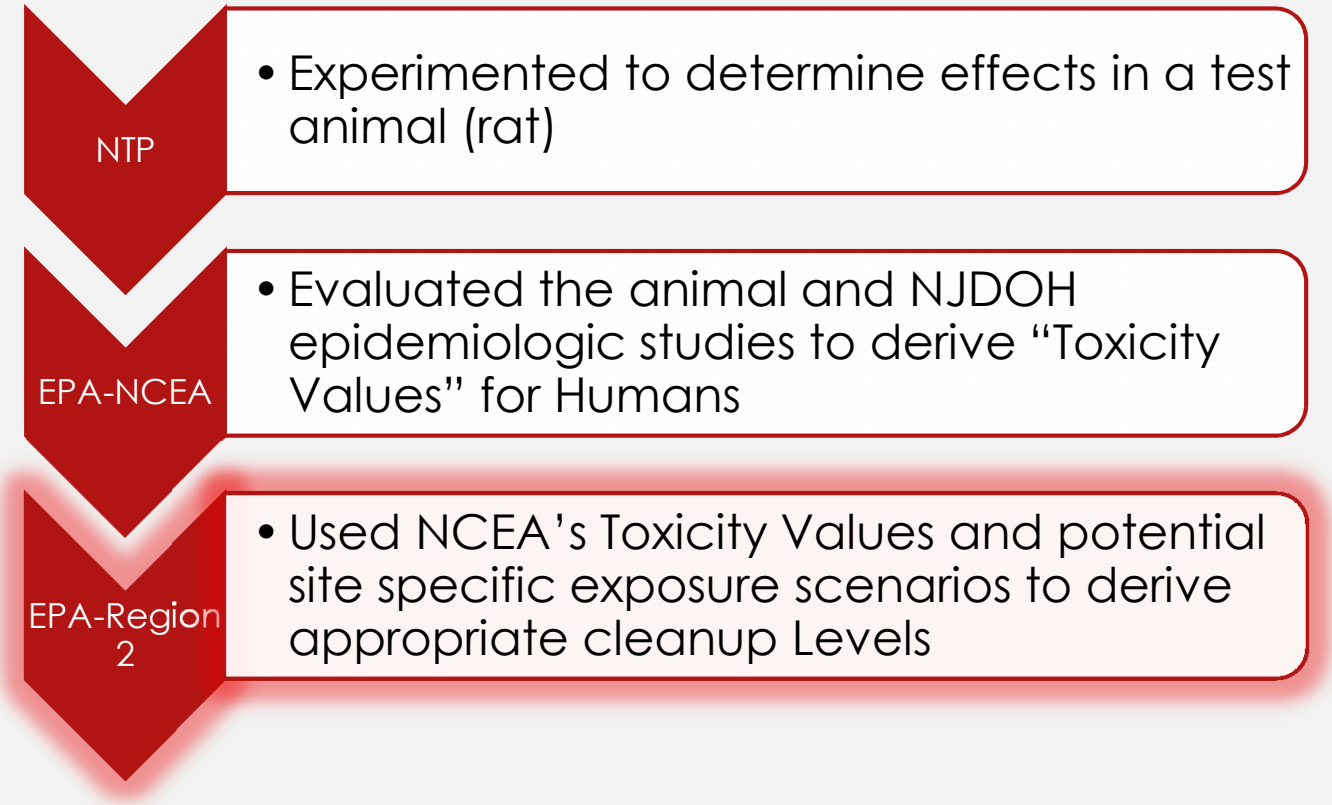

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Cleanup Level – SAN Trimer

Marian Olsen – Region 2

February 4, 2015

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Presentation Overview

- *Requirements for Cleanup Levels*
- *Toxicity Values*
- *Exposure Assumptions*
- *Calculated Cleanup Levels*
  - *Soil*
  - *Groundwater*

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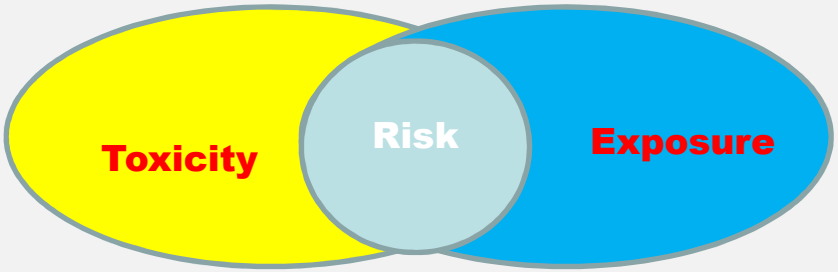
U.S. EPA Superfund Risk Assessment



- Evaluates current and future conditions
- Evaluates exposures in the absence of institutional or other controls
- Goal is health protection under reasonable maximum exposure

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Toxicity Values

- Provisional Peer-Reviewed Toxicity Values
  - *Developed by the National Center for Environmental Assessment (Lynn and Scott)*
  - *Based on Data from NTP (Mamta and Susan)*
- Oral Reference Dose or RfD
  - *0.003 milligrams/kilograms-day*

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Exposure Factors for Groundwater - Ingestion

$$C = \frac{RfD \times (BW \times AT) * CF}{IR \times EF \times ED}$$

EXPOSURE FACTORS	VALUES
Concentration (micrograms/Liter or ppb)	Value being calculated
Reference Dose (RfD)	0.003 milligrams/kilogram-day
Bodyweight (BW)	80 kilograms (176.4 lbs) Adult 15 kilograms (33.1 lbs) Child
Averaging Time (AT)	365 x ED
Conversion Factor (CF)	1000 micrograms/milligram
Ingestion Rate (water) (IR)	2.5 Liters/day (0.66 Gallons) Adult 0.78 Liters/day (0.2 Gallons) Child
Exposure Frequency (EF)	350 Days/Year
Exposure Duration (ED)	20 Years for Adult 6 Years for Child

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Exposure Factors for Soil - Ingestion

$$C = \frac{RfD \times (BW \times AT)}{IR \times EF \times ED \times CF}$$

EXPOSURE FACTORS	VALUES
Concentration (milligrams/kilogram or ppm)	Value being calculated
Reference Dose (RfD)	0.003 mg/kg-day
Bodyweight (BW)	80 kilograms (176.4 pounds) Adult 15 kilograms (33.1 pounds) Child
Averaging Time (AT)	365 x ED
Ingestion Rate (soil) (IR)	100 milligrams/day Adult 200 milligrams/day Child
Exposure Frequency (EF)	350 days/year
Exposure Duration (ED)	20 years Adult /6 Years Child
Conversion Factor (CF)	10^{-6} kilograms/milligram

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Exposure Factors for Soil - Dermal

$$C = \frac{RfD \times (BW \times AT)}{SA \times AF \times EF \times ED * ABS_d \times CF}$$

EXPOSURE FACTORS	VALUES
Concentration (mg/kg or ppm)	Value being calculated
Reference Dose (RfD)	0.003 milligrams/kilogram-day
Bodyweight (BW)	80 kilograms (176.4 lbs adult / 15 kilograms (33.1 lbs) Child
Averaging Time (AT)	365 x ED
Surface Area (cm^2) (SA)	6,032 square centimeters Adult 2,690 square centimeters Child
Adherence Factor (square centimeters) (AF)	0.07 milligrams/square centimeter Adult 0.2 milligrams/square centimeter Child
Exposure Frequency (EF)	350 days/year
Exposure Duration (ED)	20 years for Adult / 6 years for Child
Dermal Absorption Factor (ABS_d)	0.1 (default value for semi-volatile chemicals)
Conversion Factor (CF)	10^{-6} kilograms/milligram

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Calculated Cleanup Values

Receptor	Ingestion (Groundwater)	Ingestion (Soil)	Dermal (Soil)	Cleanup Level
Child	60 ug/l or ppb			
Child		235 mg/kg or ppm	870 mg/kg or ppm	185 mg/kg or ppm
Adult	100 ug/l or ppb			
Adult		2,500 mg/kg or ppm	5,930 mg/kg or ppm	1,760 mg/kg or ppm
Child – soil				185 mg/kg or ppm
Child - groundwater				6o ug/l or ppb

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Example of Calculated Values

$$\text{Cleanup Values} = \frac{1}{\frac{1}{\text{Soil ingestion value}} + \frac{1}{\text{Dermal Ingestion Value}}}$$

$$= \frac{1}{1/235 + 1/872}$$

$$= 185 \text{ mg/kg or ppm}$$

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Final Cleanup Levels

- *Groundwater – 60 ug/l or ppb*
- *Soil – 185 mg/kg or ppm*

1998 ESD: SAN Trimer must be removed from GW to “non-detect levels.”

2003 NJDOH/ATSDR Completes Epi. Study

2012 NTP Completes Animal Study

2014 EPA-NCEA Develops a PPRTV (“tox value”) for SAN Trimer

2015 EPA-Region 2 Develops Site Specific cleanup levels for SAN Trimer

Next Step. EPA/NJDEP release 3rd ESD mandating SAN Trimer cleanup levels.

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Questions?